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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/574,885	03/14/2007	Martin Pera	2354/380	3366

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/574,885	PERA ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *104-182* is/are pending in the application.

4a) Of the above claim(s) *104-108 and 123-169* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *109-122 and 170-182* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 April 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/04/09; 12/05/08; 04/07/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 03/25/09 is acknowledged.

Claims 104-182 are pending.

2. Applicant's election without traverse of Group II, claims 109-122 and 170-182 in the reply filed on 02/04/09 is acknowledged.

Claims 104-108 and 123-169 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 109-122 and 170-182 drawn to a detector of a cell type which identifies on the cell type a cell marker, characterized by binding to a GCTM-5 antibody are under consideration in the instant application.

3. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed.*

5. Claims 109-122 and 170-182 are objected to as being dependent on non-elected claim 104

Appropriate correction is required.

6. The following is a quotation of the appropriate paragraphs of U.S.C. §101 that form the basis for the rejections under this section made in this Office action:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 109-113, 115 -119 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 109-113 and 115-119 as written, do not sufficiently distinguish over nucleic acids, proteins, cells and antibodies as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as disclosed on page 29 of specification. See MPEP 2105.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 109-113, 115-121, 170-175, 177-181 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 109-113, 115-121, 170-175, 177-181 are indefinite in the recitation of " GCTM-5 antibody " because its characteristics are not known. The use of " GCTM-5 antibody " as the sole means of identifying the claimed antibody and hybridoma renders the claim indefinite because " GCTM-5 " is merely a laboratory designation which does not clearly define the claimed product, since different laboratories may use the same laboratory designation s to define completely distinct hybridomas or cell lines .

Applicant should amend the claim to provide a ATCC deposit accession number or other means of distinctly claiming the referenced antibody.

10. Also an issue is that claims 117 ,172 and 178 are indefinite in the recitation of " a stem cell selected from the group consisting of a hepatic cancer cell and pancreatic cancer cell". It is noted that said cells are differentiated cell and thus cannot be undifferentiated stem cells.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

13. In claims 114, 122, 176 and 182 it is apparent that the hybridoma cells line is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If they are not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the pertinent hybridomas which produce these antibodies. See 37 CFR 1.801-1.809.

It is noted that the specification on page 31, indicates that hybridoma which produces a GCTM-5 antibody has been deposited with the ECACC.

If the deposit have been made under the terms of the Budapest treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the **hybridoma** has been deposited under the Budapest Treaty and that the **hybridoma** will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808.

If the deposit has not been made under the Budapest treaty, then an affidevit or declaration by Applicants or someone associated with the patent owner who is in position to make such assurances, or statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met

14. Claims 109-113, 115-121, 170-175, 177-181 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : A hybridoma which produces a GCTM-5 antibody deposited with ECACC , accession number 03101603 and a kit comprising said antibody.

Applicant is not in possession of : Any detector of a cell type which is any GCTM-5 antibody or active fragment thereof.

The claimed invention is drawn to a genus of antibody that recognize a stem cell marker, which migrate on a SDS-Page gel with an apparent molecular weight of 50 kDA. The specification provide no a *per se* structure or any specific chemical and physical properties of said cell surface marker other than its apparent molecular weight. It is well known in the art that discrepancies in the art of molecular weight determination are common depending on the particular method used, e.g. whether by sodium dodecyl sulphate polyacrylamide gel electrophoresis, gel filtration or some other method, see for example Banks et al. (Eur J Biochem. 1976 Dec 11;71(2):469-73) which describes how an aspartate aminotransferase polypeptide with an expected molecule weight of 46,300 based on its primary amino acid sequence was determined to have a molecular weights of 38,000-39,500 by gel filtration with Sepadex G-100, 0.1 M NaCl; appx. 44,000 by gel filtration with Sepadex G-100, 0.4 M NaCl, 0.1 M Tris and pH 7.4; 44,130 give or take 800 by SDS-PAGE.

There is no evidence that there is any *per se* structure/function relationship between the disclosed monoclonal antibody produced by the hybridoma deposited with ECACC , accession number 03101603 and any others that might be found using the claimed method. The specification does not disclosed any amino acid sequences of stem cell marker recognized by said antibody. The Specification only provides hybridoma of accession number 03101603 which produces a specific antibody.

Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of what a material does rather than of what it is, usually does not suffice. The patent does not more than describe the desired function of the compound called for and contains no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. Inadequate written description that merely identifies a plan to accomplish an intended result "is an attempt to preempt the future before it has arrived" *Fiers v. Revel*, 984 F.2d 1164,1171 9Fed.Cir. 1993).

The claimed composition of matter defined only by its biological activity or function is insufficient to satisfy 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Guidelines for the Examination of Patent Applications Under the 35 U.S.C.112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No.4, pages 1099-1111, Friday January 5, 2001).

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --
(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 37(c) of this title before the invention thereof by the applicant for patent.

16. Claims 109-113, 115-121, are rejected under 35 U.S.C. 102(a) as being anticipated by Schopperle et al (BBRC, 2003, pages 285-290) as is evidenced by Bost *et al*

Schopperle et al., teach an monoclonal antibodies that can binds to surface membrane protein expressed on human embrional carcinoma, a malignant stem cell of testicular tumors (see entire document, Abstract and Materials and Method in particular). Said marker is biochemically and structurally similar to another testis tumor antigen GTTM-2. It is noted that the reference is silent about the recited antibody binding to a stem cell marker characterized by binding to a GCTM-5 antibody. However, it is noted both antibodies recognized antigens derived from membrane preparation from a testicular carcinomas and thus similarity between both markers would allow for cross-reactivity of the antibodies. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind the same stem cell marker as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, mean that "specifically bind" with both proteins. Bost et al (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

17. Claims 109-113, 115-121, are rejected under 35 U.S.C. 102(b) as being anticipated by Pera et al (Differentiation, 1998, IDS) as is evidenced by Bost *et al*

Pera et al., teach an monoclonal antibodies, such as GCTM-1, GCTM-2 and GCTM-4 and GCTM-3 that can binds to surface membrane proteins expressed on human embrional carcinoma, a malignant stem cell of testicular tumors (see entire document, Abstract and Materials and Method in particular). Said marker are reported to be able to recognized a proteins with an apparent molecular weight of from 57 to 85kDA . It is noted that the reference is silent about the recited antibody binding to a stem cell marker characterized by binding to a GCTM-5 antibody. However, is it is noted that all antibodies recognized antigens derived from membrane preparation from a testicular carcinomas with similar apparent molecular weight and thus similarity between both markers would allow for cross-reactivity of the antibodies. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind the same stem cell marker as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, mean that "specifically bind" with both proteins. Bost et al (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

18. Claims 109-113, 115-121, are rejected under 35 U.S.C. 102(e) as being anticipated by WO ' 03/040355 or WO 01/98463 as is evidenced by Bost *et al*

WO'355., teaches a monoclonal antibodies, that can binds to surface membrane proteins expressed on human embryonic stem cell. Said markers are reported to have an apparent molecular weight of from 68 to 85kDA (see entire document, pages 17, 18 in particular). It is noted that the reference is silent about the recited antibody binding to a stem cell marker characterized by binding to a GCTM-5 antibody. However, it is noted that all antibodies recognized surface membrane proteins expressed on human embryonic stem cell with similar apparent molecular weight and thus similarity between both markers would allow for cross-reactivity of the antibodies. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind the same stem cell marker as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

WO'463., teaches a monoclonal antibodies, that can binds to surface membrane proteins expressed on human embryonic stem cell. Said markers are reported to have an apparent molecular weight of from 68 to 85kDA (see entire document, pages 17, 18 in particular). It is noted that the reference is silent about the recited antibody binding to a stem cell marker characterized by binding to a GCTM-5 antibody. However, it is noted that all antibodies recognized surface membrane proteins expressed on human embryonic stem cell with similar apparent molecular weight and thus similarity between both markers would allow for cross-reactivity of the antibodies. Since the office does not have a laboratory to test the reference antibodies, it is applicant's burden to show that the reference antibodies do not bind the same stem cell marker as recited in the claims. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald et al.*, 205 USPQ 594 (CCPA 1980).

As is evidenced by Bost *et al* that an antibody "cross-reacts", i.e. binds to more than one protein sequence, mean that "specifically bind" with both proteins. Bost et al (Immuno. Invest. 1988 ;17:577-586) describe antibodies which "cross-react" with IL-2 and HIV envelope protein, but establish that the binding of each protein is due to the presence of a homologous sequence in each protein in which 4-6 residues were identical (see entire document, especially the Abstract and Discussion).

The reference teaching anticipates the claimed invention.

19. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

20. Claims 170-175 and 177-181 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schopperle et al., or Pera et al., or WO ' 03/040355 or WO 01/98463 each in view of U.S. Patent No. 4,281,061

The teaching of Schopperle et al., or Pera et al., WO ' 03/040355 or WO 01/98463 have been discussed, supra.

Schopperle et al., or Pera et al., WO ' 03/040355 or WO 01/98463 does not teach a kit comprising a detector of a cell type which identifies on the cell type a cell marker, characterized by binding to a GCTM-5 antibody.

US Paten '061 teaches that reagents of the pharmaceutical compositions can be provided as kits as a matter of convenience , optimization and economy of the users (see col 22, line 62 - col 23, line 4 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Paten '061 to those of Schopperle et al., or Pera et al., WO ' 03/040355 or WO 01/98463 to obtain a claimed kit comprising a detector of a cell type which identifies on the cell type a cell marker, characterized by binding to a GCTM-5 antibody.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because assemble the reagents in a kit format a matter of convenience , optimization and economy of the users as taught by US Paten '061 and the detector taught by Schopperle et al., or Pera et al., WO ' 03/040355 or WO 01/98463 can be in a pack or a kit for convenience and economy.

It is noted the only active ingredient in the claimed kit is a detector of a cell type which identifies on the cell type a cell marker, characterized by binding to a GCTM-5 antibody.

Although the kits comprise instructions, there is no patentable weight given to the instructions themselves. It would have been prima facie obvious to the ordinary artisan to include a piece of paper in the kit identifying the components therein at the time the invention was made.

It is noted that the written material in the instructions is not considered to be within the statutory classes and does not carry patentable weight. See MPEP 706.03(a). Also, see In re Haller 73 USPQ 403 (CCPA 1947), where application of printed matter to old article cannot render article patentable and In re Venezia 189 USPQ 49 (CCPA 1976), where kits are drawn to the structural attributes of interrelated component parts and not to activities that may or may not occur. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. In re Casey , 152 USPQ 235 (CCPA 1967); In re Otto , 136 USPQ 458, 459 (CCPA 1963).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

21. No claim is allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571/ 272-0735

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644